

Radiotherapy for Postoperative Thoracic Lymph Node Recurrence of Non–Small-Cell Lung Cancer Provides Better Outcomes If the Disease Is Asymptomatic and a Single-Station Involvement

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Objective: Thoracic lymph node recurrence after complete resection is common in non–small-cell lung cancer but it mostly occurs along with distant metastases. The recurrent disease might be localized and curative intent radiation therapy is the treatment of choice if no evidence of hematogenous metastasis is observed. We sought to describe the outcomes of thoracic radiotherapy for thoracic lymph node recurrences.

Methods: Fifty patients who had developed thoracic lymph node recurrence after complete resection received curative intent radiotherapy between 1997 and 2009. The clinical endpoints included the tumor response, overall survival, progression-free survival, locoregional recurrence within the irradiated field, and any other recurrence.

Results: The planned total radiotherapy was completed in 49 patients with minor toxicity. The median follow-up time after radiotherapy was 41 (19–98) months among the survivors. The response to treatment was complete response in 65%, partial response in 24%, and progressive disease in 10% of the evaluated patients. The median overall survival after radiotherapy was 37.3 months. The 5-year overall survival, progression-free survival, and local control rate were 36.1%, 22.2%, and 61.1%, respectively. A multivariate analysis revealed that the absence of symptoms and the involvement of a single lymph node station were significant factors associated with a better overall survival.

Conclusions: Radiation therapy for thoracic lymph node recurrence after complete resection is safe and provides acceptable disease control. This treatment provides a better outcome if the disease is asymptomatic and has a single-station involvement. Early detection of the recurrence may thus improve the effectiveness of this treatment.

Key Words: Radiotherapy, Lymph node recurrence, Non–small-cell lung cancer.

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Recurrence after surgery is common in patients with non–small-cell lung cancer (NSCLC). Once the disease has relapsed after surgery, it is seldom curable and the median survival time after recurrence is estimated to be 8.1 to 18.7 months.^{1–3} Most recurrences occur in multiple sites including distant organs, thus chemotherapy is commonly used for this systemic state of the disease.⁴

Thoracic lymph node recurrence is one of the exceptions when there is no evidence of hematogenous spreading of the disease. The recurrent disease might be still localized in these patients and curative intent radiation therapy is the treatment of choice.⁵ However, the efficacy and feasibility of radiotherapy for thoracic lymph node recurrence after a complete resection have not yet been clearly described. We retrospectively reviewed our experience to determine (1) progression-free survival, patterns of failure, and local control, (2) overall survival and associated factors, and (3) treatment compliance and toxicity.

PATIENTS AND METHODS

Patients

This study conducted a retrospective review of 1553 patients who underwent complete resection for NSCLC at the Osaka Medical Center for Cancer and Cardiovascular Diseases, Japan, from January 1997 to December 2009. The ethics committee gave its approval for the publication of this retrospective study. The institutional prospective database of the general thoracic department included clinicopathological variables at surgery and the postoperative clinical course. The inclusion criteria for this study were patients with lymph node recurrence as the initial recurrence, which included intrathoracic lymph nodes and supraclavicular lymph nodes and that received radiation therapy for the recurrence. Patients with any other recurrence except the thoracic lymph nodes were excluded. The method how the patients were selected from the database was shown in a CONSORT chart (Fig. 1). Finally, we identified 50 patients who received radiotherapy for thoracic lymph node recurrence. The characteristics of these patients are summarized in Table 1. There were 17 patients with thoracic lymph node recurrence who did not receive radiotherapy.

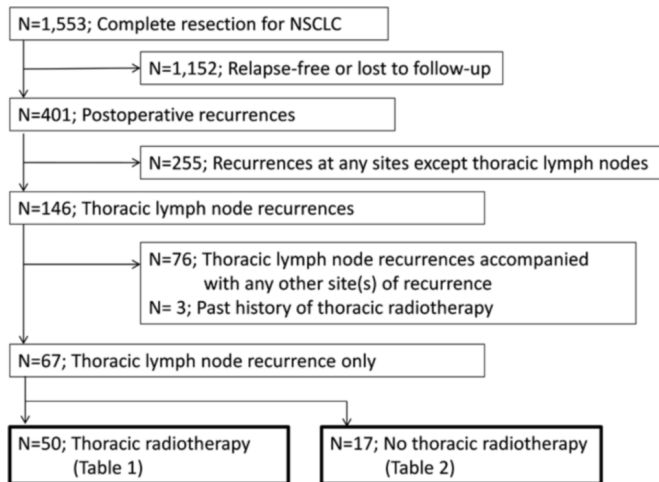


FIGURE 1. A flow chart of the patient selection. NSCLC, non-small-cell lung cancer.

The follow-up protocol for postoperative patients at this institution included a physical examination, chest radiograph, and blood testing including the value of carcinoembryonic antigen (CEA) every 3 to 6 months, and chest computed tomography (CT) every 6 to 12 months for at least 5 years. If patients were suspected of having developed recurrent disease, they were instructed to undergo systemic examinations including upper abdominal CT or abdominal echography, brain magnetic resonance imaging, and bone scintigraphy or ^{18}F -fluorodeoxy glucose-positron emission tomography (FDG-PET) before determining the treatment strategy. After undergoing thoracic radiotherapy, the patients were recommended to have more follow-up visits (every 1–3 months during the first 3 years) by surgeons and/or radiation oncologists. Six patients received concurrent systemic intravenous chemotherapy with radiotherapy.

Diagnosis of Lymph Node Recurrence

The diagnosis and status of lymph node recurrence of the patients who received radiotherapy are summarized in Table 1 ($n = 50$). The diagnosis of lymph node recurrence was based on the radiological findings of chest CT, FDG-PET, physiological examination, the value of CEA, and/or bronchoscopic sampling for cytology. Among 50 eligible patients, the cytological evidence was obtained in 10 patients (20%). Swollen lymph nodes exhibited significantly increased standard uptake values on PET scans in 31 patients (62%), and growing lymph nodes detected on at least two consecutive CT scans were observed in nine patients (18%). In these patients, radiotherapy was commenced without conducting further interventional examinations to obtain cytological evidence because lymph node recurrence was apparent on the radiological findings. The status and the treatment of recurrent diseases of the patients who did not receive radiotherapy are summarized in Table 2 ($n = 17$). There were more symptomatic diseases, more N3 level recurrences, and more multistation involvements in this group.

Protocol of Radiotherapy

The patients were treated using three-dimensional conformal techniques using a CT-based planning system (Eclipse; Varian Medical Systems, Palo Alto, CA). The gross tumor volume (GTV) was defined based on the assessment of the involved nodal region in the CT images. In addition, lymph nodes that were positive for FDG accumulation by PET/CT were included in the GTV, even if their sizes were within the normal limits on CT. The clinical target volume was defined as the GTV plus a 5-mm margin. Two different radiotherapeutic approaches, regional nodal irradiation and involved-field irradiation, were used in this study. Regional nodal irradiation covered two or more areas of five thoracic lymph node areas (right- and left-hilar areas, superior mediastinum area, supraclavicular area, and subcarinal area) in the GTV whether or not involved lymph nodes were present in the stations, whereas the involved-field irradiation covered only metastatic lymph nodes regardless of the anatomical compartment of thoracic lymph node areas. Radiotherapy was not systematically performed according to the predetermined protocol for all cases. Basically, a regional nodal irradiation approach was considered the first choice for all patients, but if the coverage of all involved stations elevated normal tissue toxicity or the patients had impaired medical conditions, the involved-field irradiation technique was applied. The treatment approach was determined on an individual basis by the experienced radiation oncologist (Table 1). Planning treatment volume denoted the clinical target volume and 5 to 15 mm margins for geometric uncertainties and respiratory motion. The prescribed dose was calculated with a heterogeneous dose calculation algorithm (pencil beam convolution or anisotropic analytical algorithm). Conventional fractionation was used (2–3 Gy per fraction) and the preplanned radiation dose ranged from 60 to 66 Gy in 43 patients. In four patients, the dose was reduced to 50 Gy because of the radiation field and/or patient's medical condition. In three patients, the dose was increased up to 70 to 84 Gy. Treatment was delivered using 6- or 10-MV photons of the linear accelerator (Clinac 2100C/23EX; Varian Medical systems). Dose prescription was defined according to International Commission on Radiation Units and Measurements recommendations.

Clinical Endpoints

Clinical endpoints after radiotherapy included the overall survival, progression-free survival, tumor response, and locoregional recurrence within the irradiated field and any other recurrence. All responses were evaluated 3 to 6 months after the completion of radiotherapy based on follow-up CT and/or PET scan. Complete response (CR) was defined as the shrinking of metastatic nodes to normal size (the longest diameter was <10 mm) on chest CT without significant accumulation of FDG on PET. The value of CEA was also required to be within the normal limit if it was elevated before the radiotherapy. Partial response required more than 30% reduction of the longest diameter. Progressive disease was defined as increase of more than 20% of the longest diameter and/or progression of any other recurrent disease. Local tumor recurrence was defined as progressive abnormal CT images within the irradiated field during the follow-up period. The time of recurrence

TABLE 1. Patient Characteristics, the Diagnosis, and Status of Lymph Node Recurrence, and Treatment Protocol of Thoracic Radiotherapy

Variables	N = 50	Univariate Analysis for Overall Survival, <i>p</i>
Age at LN recurrence, years old		0.6915 (≤ 67 vs. > 68)
Median (range)	68 (48–84)	
Sex (male/female)	42/8	0.4085
Smoking status (nonsmoker/smoker)	11/39	0.9443
Primary site		
Right/left	32/18	0.5459
Upper or middle/lower	31/19	0.7960
Surgery		
Limited resection (wedge/segmentectomy)	6 (3/3)	0.5875
Standard surgery (lobectomy/bilobectomy/pneumonectomy)	44 (39/4/1)	
Histology (adenoca/squamous/others)	21/27/2	0.5706
Stage ^a at surgery		0.5723 (I or II vs. III)
IA/IB/IIA/IIB/IIIA	11/3/10/0/26	
Disease-free interval after surgery, days		0.2965 (≤ 365 vs. > 365)
Median	324	
Range	86–3088	
Diagnostic procedure		
Patho- or cytological examination	10	
PET/CT	31	
CT (+symptom or elevated CEA)	9	
Number of stations (single/multiple)	30/20	0.0457
Site of LN recurrence		0.2331 (N1 vs. N2/N3)
N1 level		
Ip–hilar only	10	
N2 level		
Upper med. (+ip–hilar)	19	
Lower med. (+ip–hilar)	5	
Upper and lower med. (+ip–hilar)	4	
N3 level		
SC (+upper or lower med.)	10	
Cl–hilar and upper med.	2	
Symptoms at recurrence (^b present/absent)	13/37	0.0017
Maximum diameter of involved LN (mm)		0.4784
20 or smaller/21 or larger	26/24	
Radiation approach		0.3853
Regional nodal/involved-field	23/27	
Radiation dose (Gy)		0.4325 (≤ 60 Gy vs. > 60 Gy)
50~59/60~69/70~	4/43/3	
Concurrent chemotherapy		0.6185
Yes/no	6/54	

^aThe stages were described according to the 7th edition.

^bDetails are cough in seven patients, sputum production in five patients, bloody sputum in two patients, breathlessness in two patients, and hoarseness in two patients.

LN, lymph node; PET, positron emission tomography; CT, computed tomography; Ip–hilar, ipsilateral hilar; med., mediastinal; SC, subclavicular; cl–hilar, contralateral hilar.

was recorded using the interval-censored techniques. The duration of survival and time to failure were determined from the initiation of the radiation therapy until the date of death and the time of recurrence, respectively. The patients lost to the follow-up were censored at the date of last contact with the institution. Toxicity was assessed using the National Cancer Institute Common Toxicity Criteria scale version 2.0.

Statistics

Survival was calculated by the Kaplan–Meier method, and differences in survival were assessed by a log-rank analysis. The factors whose *p* values were less than 0.10 (borderline significant) in the univariate analysis in Table 1 were further examined using a multivariate analysis. A multivariate analysis for prognostic factors was performed using the Cox

TABLE 2. The Status and the Treatment of Recurrent Diseases in the Patients Who Did Not Receive Radiotherapy

Variables		N = 17
Disease-free interval after surgery, days		482 (97–1297)
Number of stations	Single/multiple	1/16
Site of LN recurrence	N1 level	0
	N2 level	6
	N3 level	11
Symptoms at recurrence	Present/absent	9/8
Maximum diameter of involved LN	20 or smaller/21 or larger	7/10
Treatment for recurrence	Chemotherapy	10
	EGFR-TKI therapy	2
	Supportive care	5
Reason why radiotherapy was not chosen	Extensive lymph node recurrence	6
	Lung fibrosis/COPD	7
	Others	4

EGFR-TKI, epidermal growth factor receptor-tyrosine kinase inhibitor; COPD, chronic obstructive pulmonary disease; LN, lymph node.

proportional hazard regression model. *p* values less than 0.05 were considered to be statistically significant. The statistical analyses were carried out using the JMP 8 software package (SAS Institute, Cary, NC).

RESULTS

Response to Treatment

Response to treatment was evaluated in all patients but one who died of another cause 4 months after the radiation treatment. Thirty-two of 49 patients (65%) had CR, 12 (24%) had partial response, and five (10%) had progressive disease. A univariate analysis showed that there were no variables associated with the response when patients' response to treatment was divided into with CR and the others. An example of a CR is shown in Figure 2. Relief of the associated symptoms was achieved after radiotherapy in 12 of 13 symptomatic patients. There were 16 patients with elevated CEA values before radiotherapy. Among them, the CEA values responded to radiotherapy in 13 patients (81%), and nine patients (56%) exhibited normal CEA values after radiotherapy.

Progression-Free Survival, Patterns of Failure, and Local Control after Radiotherapy

The median follow-up period after radiation therapy among the survivors was 41 months (range, 19–98 months). Two patients were lost to follow-up at 50 and 73 months after radiotherapy. The remaining survivors received the follow-up per the protocol and the recommendation until this study was closed. Disease progression after radiation therapy was observed in 36 patients (72%). Progression-free survival after radiotherapy is shown in Figure 3A. The 1-, 3-, and 5-year progression-free survival rates were 49.1%, 28.2%, and 22.2%, respectively. The median progression-free interval was

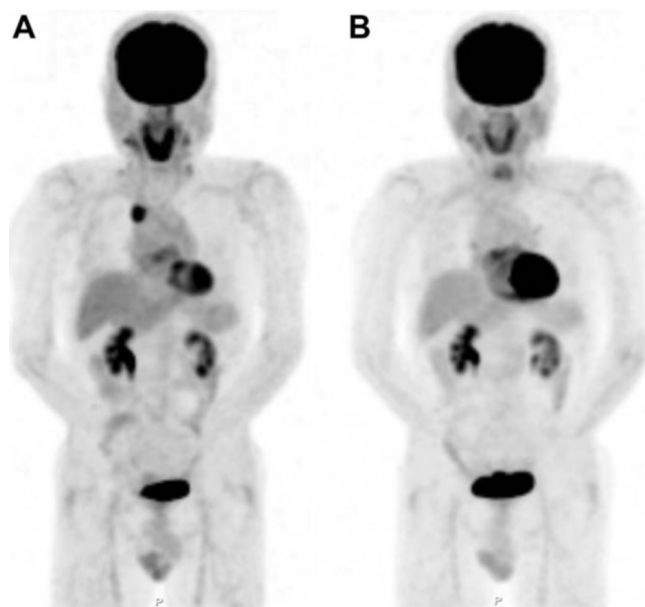


FIGURE 2. An example of complete response to radiotherapy for postoperative lymph node recurrence. PET scans of the whole body were obtained at baseline (A) and after 6 months of radiotherapy (B). PET, positron emission tomography.

12.0 months after radiotherapy. Ten (23%) of 43 patients who were followed up for more than 3 years showed no additional recurrence after radiotherapy. The initial sites of the disease progression are summarized in Table 3. In-field recurrence was observed in 18 patients (36%) during their entire follow-up period. The probability of local control is shown by the Kaplan–Meier method in Figure 3B. The 3- and the 5-year local control rates were 65.9% and 61.1%, respectively. The incidence of initial recurrence in thoracic lymph nodes and the in-field recurrence rate were not associated with the radiotherapeutic approach.

Overall Survival and Prognostic Factors after Radiotherapy

Twenty-seven patients (54%) died of lung cancer and two patients (4%) died of other causes within a 5-year follow-up period. The overall survival probability is shown in Figure 3C. The 1-, 3-, and 5-year overall survival rates were 84.0%, 52.7%, and 36.1%, respectively. The median overall survival was 37.3 months after radiotherapy. A univariate analysis was used to evaluate the prognostic impact of 16 clinicopathological factors listed in Table 1. The absence of symptoms and a single involved lymph node station at recurrence were significant favorable prognostic factors but others were not. A multivariate analysis showed that the absence of symptoms and single involved lymph node station were significant independent factors associated with the overall survival (Table 4). The median overall survival was 45.4 months for nonsymptomatic patients and 48.9 months for patients with a single involved lymph node station. There were 23 patients (46%) patients who were both nonsymptomatic and with single involved

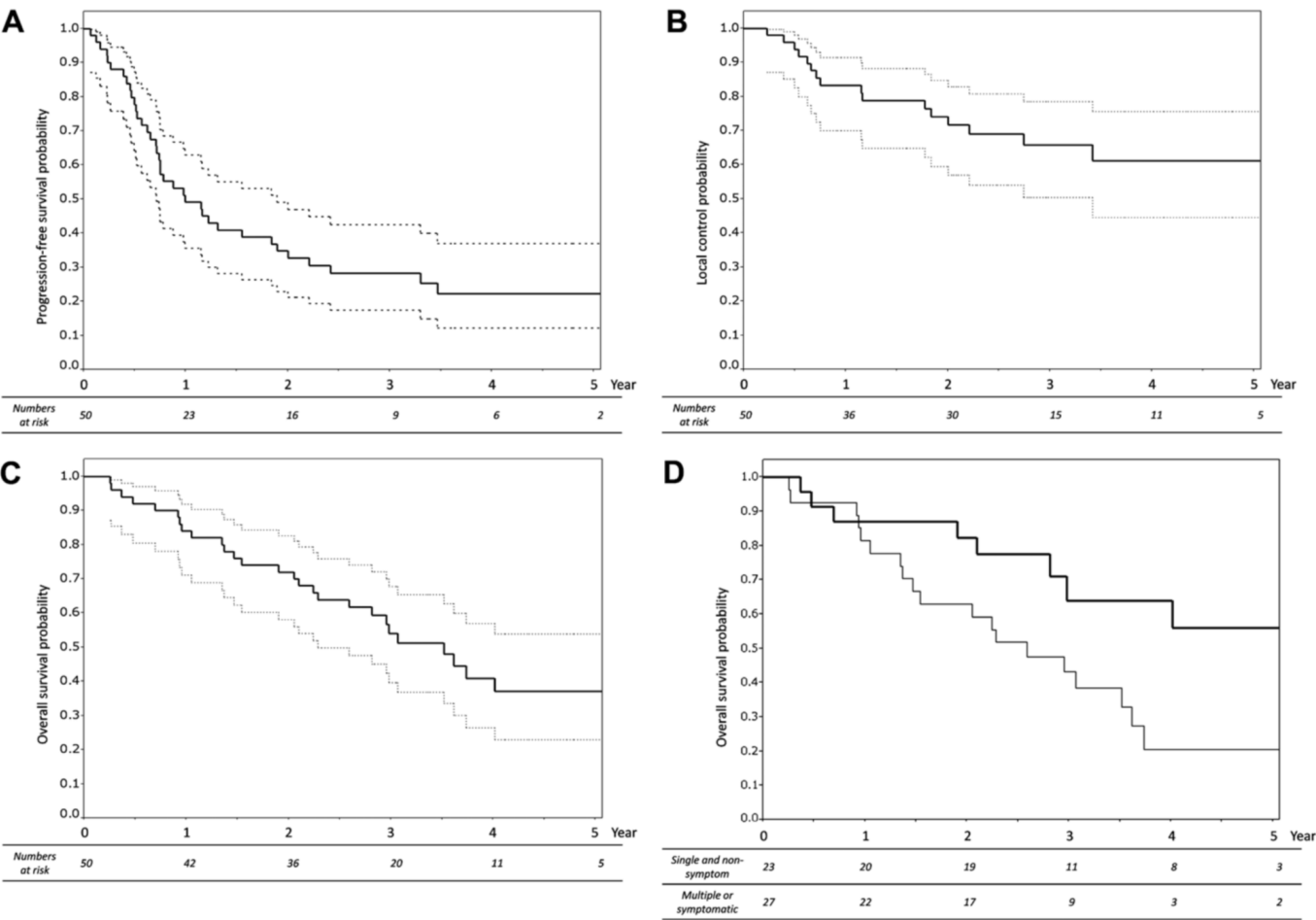


FIGURE 3. Plots of the progression-free survival (A), local control (B), and overall survival (C) probabilities with 95% confidence intervals (dash lines) among patients who received radiotherapy for thoracic lymph node recurrence after surgery. Plots of the overall survival (D) probabilities in the patients who were both nonsymptomatic and with single involved lymph nodes station ($n = 23$, bold line) and the patients who were symptomatic or with multiple involved lymph nodes stations ($n = 27$, faint line).

lymph nodes station. The overall survival probability of those patients and the remaining patients are shown in Figure 3D. The initial sites of the disease progression were not associated with these factors. The use of concurrent chemotherapy did not affect the overall or progression-free survival. There were five patients who had single-station lymph node recurrence in the supraclavicular area. Two of these patients survived more than 3 years after radiotherapy without any other disease recurrences.

Treatment Compliance and Toxicity

The planned total radiotherapy dose was delivered to 49 patients (98%) of 50 patients. One patient (2%) developed grade 2 pneumonitis and esophagitis at 56 Gy/60 Gy and refused further therapy. The remaining patients showed acute toxicity of grade 2 in six patients (12%) (esophagitis, pneumonitis, malaise, and arthralgia), acute toxicity of grade 3 in one patient (2%; dyspnea), and late toxicity of grade 3 in one patients (2%; pneumonitis). Grade 3 toxicities were observed in patients receiving regional nodal radiotherapy.

Overall Survival of the Patients Who Did Not Receive Radiotherapy

The overall probability of survival of the patients who did not receive radiotherapy is shown in Figure 4. The median survival was 443 days, and the 1-year and the 3-year survival probabilities were 58.8% and 5.9%, respectively.

DISCUSSION

Many of the patients who undergo radical resection for NSCLC develop recurrence with a dismal prognosis. The use of chemotherapy is generally recognized as a standard option to provide objective responses and small improvement in survival for patients with recurrent disease just as performed for initial stage IV patients.

Postoperative lymph node recurrence is common but it mostly occurs along with distant metastases.⁴ Systemic therapy would be indicated for patients with recurrences in both lymph nodes and a distant organ. However, the disease is considered to be localized if thoracic lymph nodes are involved but no other metastasis is observed after systematic workup,

TABLE 3. Initial Site of Disease Progression after Radiotherapy

Site	Number of Patients
Pulmonary metastasis or pleural dissemination	11
Extrathoracic distant metastasis	7
Lymph nodes out of the radiation field	9
Lymph nodes within the radiation field	9
Alive without the disease	14

TABLE 4. Multivariate Analysis of Overall Survival after Radiotherapy

Variable	Reference	HR	95% CI	<i>p</i>
Symptom	Absent	3.86	1.72–8.57	0.0014
Number of stations	Single	2.70	1.21–6.12	0.0152

Cox proportional hazard model.
HR, hazard ratio; CI, confidence interval.

and these patients may have a chance to be cured. A report of the anatomic location of NSCLC recurrences in 378 patients showed that there were 30 mediastinal lymph node recurrences (7.9%).⁶ Curative intent radiotherapy can be indicated for this specific state of the disease. The database of this institution yielded 50 patients who underwent thoracic radiotherapy in this setting, and the short- and the long-term outcomes of this treatment were analyzed. The treatment was completed in most of the patients and no serious complications were recorded. The median overall survival was 37 months and the 5-year survival rate was 36.1%. Ten (20%) of 50 patients were alive longer than 3 years without any additional recurrence after the radiotherapy. These results suggest that a subset of patients with postoperative lymph node recurrence may be cured or enjoy a long-lasting progression-free survival by thoracic radiotherapy.

To date there have been few reports that summarize the treatments for recurrent disease in the literature.^{1–3,7} Previous reports show that the median postrecurrent survival ranges from 8.1 to 18.7 months. Limiting the results to the patients who underwent radiotherapy for lymph node recurrence or other locoregional recurrence shows a median survival after recurrence of 14 to 15 months.^{5,8–10}

The CEA values were used for monitoring the treatment effects in this study. The normal CEA values were required for the CR definition after radiotherapy, although the use of CEA in NSCLC remains controversial. Several reports have indicated that elevated serum CEA levels are associated with an unfavorable prognosis and occult lymph node metastasis in NSCLC patients.^{11,12} Indeed, we observed several patients whose lymph nodes shrank to normal size by radiotherapy but their CEA levels were still elevated comparing with the normal limit. By using the size criteria only, we might overestimate the CR rate.

The outcomes in the current study were favorable as a treatment for recurrent disease. The CR rate was as high as 65%. The median survival and the 5-year survival rate in the present series were considerably longer than those of previous reports.^{5,8–10} This is partially because of significant improvements in conformal radiotherapy within the past one or two decades, which have enabled the use of intensive radiotherapy to treat recurrent disease with less radiation toxicity. Another reason may exist in the differences in patient backgrounds. More patients with associated symptoms were included and the size of the recurrent tumor was larger in the previous studies. In contrast, the disease was nonsymptomatic, the involved lymph nodes were localized in only one station, and the size of the target tumor was smaller than 30 mm in many of the patients in this study.

The prognostic impact of variables was evaluated by univariate and multivariate analyses to select the patients who may benefit most from this treatment. The analysis revealed

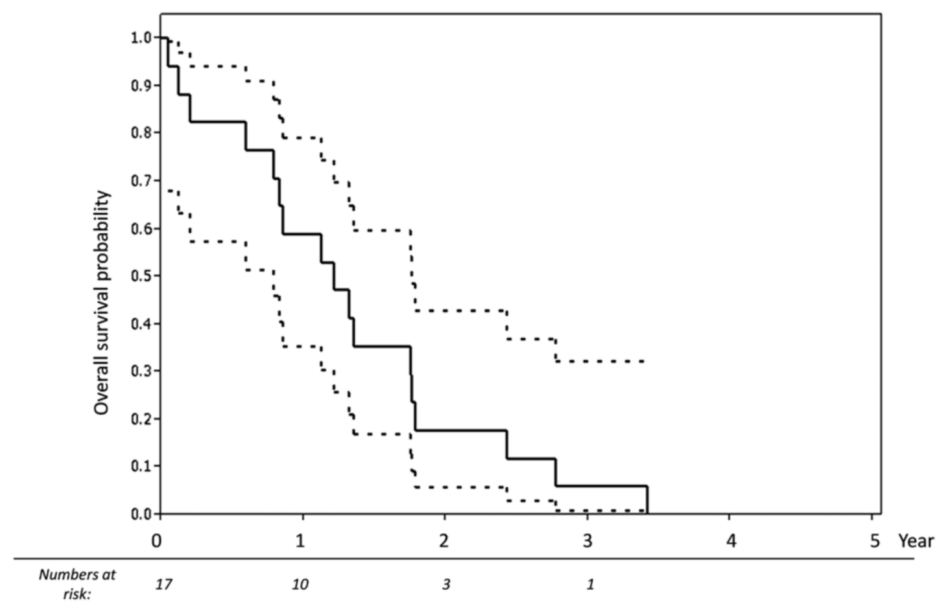


FIGURE 4. Plots of the overall survival probabilities with 95% confidence intervals (dash lines) among patients who did not receive radiotherapy ($n = 17$).

that absence of symptoms at the time of recurrence and a single involved lymph node station were favorable prognostic indicators after recurrence. Interestingly, both prognostic factors in this study were associated with early presentation of recurrence. The surveillance program in this institution, which includes chest CT one or two times a year is relatively intensive in comparison with the guideline-recommended programs.¹³ PET scan was also useful, because PET distinguished thoracic lymph node recurrence from nonspecific postoperative change. The intensive surveillance using chest CT and PET may play an important role in the early diagnosis of lymph node recurrence. The results of the present study and the comparisons with previous studies suggest that early detection of recurrence after surgery may contribute to achieving good disease control after radiation and, as a result, longer survival.

A favorable local control rate within the irradiated field was obtained by thoracic radiotherapy without any severe adverse events. The radiation dose prescribed in this study was considered to be adequate. Radiotherapeutic approaches in this study were classified into regional nodal irradiation and involved-field irradiation. Regional nodal radiation therapy covers a larger field and, as a result, may allow more irradiation to adjacent organs such as lung and esophagus, in comparison with involved-field radiation, which targets only metastatic nodes. Local recurrence-free survival or patterns of failure after radiotherapy were not associated with the choice of the radiation approach. On the basis of this result, restricting the target volume to the involved nodal regions might be an option as a radiation approach for thoracic lymph node recurrence. These phenomena were similarly observed in the comparison between elective nodal irradiation and involved-field irradiation for locally advanced unresectable NSCLC.^{14,15}

Systemic chemotherapy is a mainstay of treatment for recurrent NSCLC. Only a small number of patients received concurrent chemotherapy in this study. Considering that concurrent chemoradiotherapy is a standard treatment for the patients with inoperable stage III NSCLC, this approach can be another option for regional lymph node recurrence after surgery. When selecting the treatment strategy for patients with thoracic lymph node metastases, it should be noted that there were essential differences between stage III NSCLC and postoperative recurrences. First, the primary tumor had been resected in postoperative patients. Second, the nodal disease was observed after at least a few months of disease-free status. In addition, the sizes of involved lymph nodes were relatively small and their distribution was limited to a couple of stations in most of the recurrent patients. Therefore, thoracic lymph node recurrences were considered to be local disease, and curative intent radiation therapy was the treatment of choice. In contrast, the involved lymph nodes in inoperable stage III patients are usually bulky and extended to multiple nodal stations. Consequently, the prognostic advantage was not observed in the patients who received concurrent chemotherapy. However, because distant metastasis or pleural dissemination was the initial site of the disease progression in 18 patients (36%), the use of

chemotherapy may thus have additional effects on controlling the subclinical systemic disease.

The strength of this study is that as a single-institutional study it provided complete information on the clinical course after surgery including recurrence, failure after radiotherapy, final outcomes, well-controlled planning, and quality of radiotherapy.

There are limitations that need to be acknowledged. This study may include the patients whose involved lymph nodes were relatively limited in terms of their number and their location. Because this retrospective analysis was inherently affected by a selection bias associated with the use of radiotherapy, a straightforward comparison between the patients who received radiotherapy and the patients who did not receive radiotherapy was not allowed. Therefore, the real possible benefits of radiotherapy for thoracic lymph node recurrence over chemotherapy alone remain uncertain. Another limitation, as in other studies of nonsurgical therapies, is the lack of a pathological diagnosis. Lymph node sampling under mediastinoscopy or thoracotomy is usually impossible or is a high-risk procedure because systematic mediastinal lymph node dissection is generally performed during the initial surgery. Accurate targeting of an involved lymph node by endobronchial ultrasound-guided transbronchial needle aspiration requires technical skills and experience because the anatomy in the mediastinum was affected by surgery. FDG-PET was used to make a diagnosis in 31 of 40 patients without pathological evidence; however, it was not available in the remaining nine patients. Even though FDG-PET shows good diagnostic performance in detecting recurrence in postoperative NSCLC patients with a fairly high sensitivity (97%) and specificity (96%) as seen in our previous report,¹⁶ we could not eliminate the possibility of false-positive diagnoses in our study. In addition, the sample size of this study was relatively small because this type of recurrence is uncommon. Despite these essential shortcomings, the data demonstrated the favorable results of radiotherapy for patients whose characteristics were described in this study.

In conclusion, radiation therapy for thoracic lymph node recurrence after complete resection is safe and provides acceptable disease control. This treatment provides better outcomes if the disease is asymptomatic and has a single-station involvement. Early detection of thoracic lymph node recurrence may therefore improve the effectiveness of this treatment strategy.

REFERENCES

1. Hishida T, Nagai K, Yoshida J, et al. Is surgical resection indicated for a solitary non-small cell lung cancer recurrence? *J Thorac Cardiovasc Surg* 2006;131:838–842.
2. Sugimura H, Nichols FC, Yang P, et al. Survival after recurrent nonsmall-cell lung cancer after complete pulmonary resection. *Ann Thorac Surg* 2007;83:409–17; discussion 417.
3. Endo C, Sakurada A, Notsuda H, et al. Results of long-term follow-up of patients with completely resected non-small cell lung cancer. *Ann Thorac Surg* 2012;93:1061–1068.
4. Boyd JA, Hubbs JL, Kim DW, Hollis D, Marks LB, Kelsey CR. Timing of local and distant failure in resected lung cancer: implications for reported rates of local failure. *J Thorac Oncol* 2010;5:211–214.

5. Jeremic B, Shibamoto Y, Milicic B, et al. External beam radiation therapy alone for loco-regional recurrence of non-small-cell lung cancer after complete resection. *Lung Cancer* 1999;23:135–142.
6. Taylor MD, Nagji AS, Bhamidipati CM, et al. Tumor recurrence after complete resection for non-small cell lung cancer. *Ann Thorac Surg* 2012;93:1813–20; discussion 1820.
7. Nakagawa T, Okumura N, Ohata K, Igai H, Matsuoka T, Kameyama K. Postrecurrence survival in patients with stage I non-small cell lung cancer. *Eur J Cardiothorac Surg* 2008;34:499–504.
8. Kagami Y, Nishio M, Narimatsu N, et al. Radiotherapy for locoregional recurrent tumors after resection of non-small cell lung cancer. *Lung Cancer* 1998;20:31–35.
9. Leung J, Ball D, Worotniuk T, Laidlaw C. Survival following radiotherapy for post-surgical locoregional recurrence of non-small cell lung cancer. *Lung Cancer* 1995;13:121–127.
10. Tada T, Fukuda H, Nakagawa K, et al. Non-small cell lung cancer: radiation therapy for locoregional recurrence after complete resection. *Int J Clin Oncol* 2005;10:425–428.
11. Grunnet M, Sorensen JB. Carcinoembryonic antigen (CEA) as tumor marker in lung cancer. *Lung Cancer* 2012;76:138–143.
12. Koike T, Koike T, Yamato Y, Yoshiya K, Toyabe S. Predictive risk factors for mediastinal lymph node metastasis in clinical stage IA non-small-cell lung cancer patients. *J Thorac Oncol* 2012;7:1246–1251.
13. Rubins J, Unger M, Colice GL; American College of Chest Physicians. Follow-up and surveillance of the lung cancer patient following curative intent therapy: ACCP evidence-based clinical practice guideline (2nd edition). *Chest* 2007;132(3 Suppl):355S–367S.
14. Perez CA, Stanley K, Grundy G, et al. Impact of irradiation technique and tumor extent in tumor control and survival of patients with unresectable non-oat cell carcinoma of the lung: report by the Radiation Therapy Oncology Group. *Cancer* 1982;50:1091–1099.
15. Rosenzweig KE, Sura S, Jackson A, et al. Involved-field radiation therapy for inoperable non-small cell lung cancer. *J Clin Oncol* 2007;25:5557–5561.
16. Kanzaki R, Higashiyama M, Maeda J, et al. Clinical value of F18-fluorodeoxyglucose positron emission tomography-computed tomography in patients with non-small cell lung cancer after potentially curative surgery: experience with 241 patients. *Interact Cardiovasc Thorac Surg* 2010;10:1009–1014.